Texila International Journal of Public Health
ISSN: 2520-3134
DOI: 10.21522/TIJPH.2013.12.02.Art012

Prevalence of HIV among Drug Resistance Tuberculosis Cases at the National Tuberculosis and Leprosy Training Centre Zaria

Bitrus Joshua Barde[1*], Joseph Okopi[2], Isiyaku Ahmadu[3]
[1]*Department of Public Health, Texila American University, Georgetown, Guyana*
[2]*Department of Microbiology, Federal University of Health Sciences, Otukpo Benue State, Nigeria*
[3]*National Tuberculosis and Leprosy Training Centre, Saye-Zaria, Kaduna State, Nigeria*

Abstract

While multi-drug resistant Tuberculosis (MDR-TB) remains a threat to the global fight for the elimination of Tuberculosis (TB), HIV coinfection with MDR-TB makes TB management even worse. Previous studies have reported poorer outcomes and staggering high mortality rates among persons coinfected with HIV and MDR-TB. This coinfection is said to be the leading cause of many MDR-TB-related outbreaks. However, there has been a great decline in the mortality rates reported due to the treatment of HIV with antiretroviral drugs and anti-TB drugs for MDR-TB. Coinfection of HIV and MDR-TB has high prevalence rates in certain regions of the world, including Nigeria. This study assessed the prevalence of HIV among drug-resistant TB patients attending the National Tuberculosis and Leprosy Training Centre (NTBLTC), Saye, to contribute to knowledge and data repository which is limited in this area. This cross-sectional study involved 135 GeneXpert MTB/RIF-screened patients. Blood samples for HIV testing were collected from patients who consented while sputum samples collected were analysed by GeneXpert MTB/RIF and Molecular Line Probe Assay. The results of this study showed an overall HIV prevalence rate of 35.6% ($p<0.05$) among GeneXPert MTB/RIF-positive confirmed TB subjects.HIV incidence rates among different drug-resistant groups were as follows; mono-resistant TB 19(14.1%), MDR-TB 16(11.9%) and Poly-resistance was determined to be 2 (1.5%) respectively.

Keywords: *Human Immunodeficiency Virus, Multi-drug Resistance, Mycobacterium tuberculosis, Tuberculosis.*

Introduction

Mycobacterium tuberculosis causes an infectious bacteriological disease called tuberculosis (TB), which poses a serious public health challenge to developing countries including Nigeria. Coinfection with TB and HIV remains a grave public health concern of global magnitude due to the high mortality rates recorded [1]. In 2013 alone, nine million TB cases were reported out of which 13% were infected with HIV and Africa had the highest burden of HIV/TB coinfection rates of up to 13% [2]. Tuberculosis is spread by inhaling tiny droplets released when infected people cough or sneeze. Although only a small percentage of people infected with Mycobacterium tuberculosis develop tuberculosis, it remains a cause of disability and death worldwide. Clinical symptoms include cough, fatigue, fever, weight loss, hoarseness, chest pain, and hemoptysis (bloody sputum). Although tuberculosis incidence and mortality declined in several countries, including Nigeria, in the mid-20th century, there has been a resurgence in the last decade. Several researchers both in Nigeria

Received: 06.04.2024 ***Accepted: 20.05.2024*** ***Published on: 28.06.2024***
****Corresponding Author: bity2002ng@yahoo.com***

and abroad attributed this recovery to the HIV/AIDS epidemic [1,2,3,4,27,28]. This connection is confirmed by the simultaneous increase in the incidence of tuberculosis and the emergence of AIDS in many countries [3,4]. It should be noted that the risk of developing tuberculosis is significantly higher in those infected with HIV. Although tuberculosis is a treatable disease, it still kills about 5,000 people per day and about 1.7 million per year [5]. The disease disproportionately affects vulnerable communities, particularly the poorest and most malnourished, and is closely linked to overpopulation, limited access to free or low-cost health services, and reliance on traditional healers, which facilitate the transmission of tuberculosis [2].

Globally, the incidence rate of tuberculosis continues to increase at 1% per year, with the incidence of multidrug-resistant (MDR) tuberculosis increasing, particularly in Africa. Tuberculosis is the second leading cause of death from infectious diseases worldwide after human immunodeficiency virus (HIV) [6]. It is estimated that there were up to nine million fresh cases of tuberculosis in 2013. There have been 5 million deaths due to tuberculosis, with most cases and deaths occurring in men. In addition, 1 million children contracted tuberculosis and 140,000 children died in 2014. Tuberculosis remains a major infectious disease worldwide, causing 9.6 million illnesses and 1.5 million deaths in 2014[2].

In Nigeria, tuberculosis remains a major public health problem, ranking tenth in the world out of 22 countries with high rates of tuberculosis and fourth in Africa. The 2015 Global TB Report highlighted estimates of the high burden of disease in Nigeria, with prevalence and incidence rates of 330 and 322 per 100,000 population respectively. The mortality rate for tuberculosis (excluding HIV+TB) was 97, while the mortality rate for HIV+TB was 44. These figures are alarming, considering that most deaths could be prevented through timely access to health care for diagnosis and appropriate treatment [7,8].

Even though HIV is a potent risk factor for the occurrence of all types of TB and MDR-TB among persons living with HIV, population-based statistics on the relationship between MDR-TB and HIV infection remain limited [2]. This study was therefore aimed at determining the prevalence of HIV among drug-resistant TB subjects attending the NTBLTC and by so doing contribute to knowledge and to bridge the information deficit in this area.

Materials and Methods

The research was carried out at the National Tuberculosis and Leprosy Training Center (NTBLTC) located in Saye, Zaria on the old Kaduna-Zaria Road, Kaduna State - Nigeria. The center also houses the second national reference laboratory for tuberculosis in the North West of Nigeria. The Center's responsibilities include training staff under the National TBL Control Program (NTBLCP), providing tuberculosis, HIV and leprosy services (diagnosis, chemotherapy, etc.) and operational research on tuberculosis, HIV and leprosy. NTBLTC Saye, based in Zaria, Kaduna State, Nigeria, is an important institution in the fight against tuberculosis and leprosy. The National Tuberculosis Reference Laboratories (NTRL) is recognized as the leading tuberculosis reference center in Northern Nigeria. The NTRL offers biosafety levels 2 and 3 (BSL 2 and 3) and is equipped with advanced facilities. Patients with suspected tuberculosis were included in the study and unsuspected subjects were excluded. Ethical approval was duly obtained from the health research ethics committee of the center.

This study was conducted between August 2022 and November 2023 on hundred and thirty-five (135) sputum and blood samples from patients who attended the National Tuberculosis and Leprosy Training Center clinic in Saye-Zaria. The sample size was

calculated based on a national prevalence rate of 590,000 inhabitants out of a current population estimated at 177,476,000 inhabitants [7].

Sample Collection

Samples were collected from 135 GeneXpert MTB/RIF-detected individuals, having pulmonary tuberculosis who consented. All 135 sputum samples were collected as spot samples in line with recent TB guidelines for routine laboratory investigations for TB suspected patients. All samples collected were pre-treated (digested, homogenized, decontaminated and concentrated) in a Biosafety level II cabinet using reagents and methods as described in the NTBLTC manual. Detailed patient Biodata and laboratory-specific information was recorded on a standardized case record form and captured on Excel using double data entry.

Sample Analysis

GeneXpert MTB/RIF

All Acid-Fast Bacilli-positive samples were further analysed using GeneXpert MTB/RIF to detect Rifampicin-positive samples. The test was for confirming the presence of M. tuberculosis and resistance TB using the Nucleic Acid Amplification Test (NAAT) powered by the GeneXpert MTB/RIF analyser. The test was a semi-nested rt-PCR reaction conducted following the manufacturer's instructions [9].

Line Probe Assay

All sputum samples were further tested for resistance to second-line drugs utilizing the Genotype MTBDRsl/Line probe assay (Hain Life Science GmbH, Nehren, Germany). The processes included DNA extraction procedure with genolyse, PCR amplification of the extracted DNA and hybridization followed by detection. Line probe assay analysis strictly followed the guidelines provided by the manufacturers [10].

HIV Diagnosis

HIV counselling services were given to participants before testing. Testing for detection of HIV antibodies was conducted on all 135 study participants who consented to be tested. The national algorithm for HIV testing was used with the test kit as the front-line test, Unigold as the second line and Stat Pak rapid diagnostic test kits as the tiebreaker, HIV testing was carried out in line with the manufacturer's instructions. All HIV reactive results by Determine test kits were further retested with Unigold test kits and if reactive were reported as positive. In the event of a discordant result from Determine and Unigold, a third line of test known as Stat Pak was used to serve as the tiebreaker. For a test to be reported as being positive, at least two of the three HIV rapid screening assays must be reactive [11].

Data Analysis

Statistical analysis was conducted using both Excel and Statistical Package for Social Science (SPSS) version 20. The test of significance was set at $p<0.05$.

Results

A total of 135 GenXpert MTB/RIF confirmed subjects comprising 93(68.9%) males and 42 females were tested for HIV seropositivity. Of the 135 confirmed cases of drug-resistant TB 48 were coinfected with HIV. Table 1 shows the Prevalence of HIV among DR-TB at NTBLTC Zaria which was determined to be 35.6%. Distribution of HIV among patients about sex shown in Table 2 showed that of the 93 males in the study population, 31(23.0%) were HIV Seropositive while 17(12.6%) out of the 42 females were seropositive, indicating high seropositivity among males. Table 3 shows the distribution of HIV+DR-TB among Patients by Age Demographics the majority of the HIV seropositive cases among the study subjects were in the age range of 20-29 years

representing a total of 19 (14.1%) of the study population. This is followed by the age group 30 – 39 with 14 (10.4%) patients. The age group with the least number of HIV cases were age range 50- 59 with 9(6.7%) and 40-49 with 6 (4.4%). Age ranges 01 – 09 and 60 - 69 both recorded no incidence of HIV positive cases.

Table 4 shows the comparison of HIV Prevalence among drug-resistant TB in the Study Population**.** The rate of coinfection based on the type of TB drug resistance showed that 29 Mono-resistant TB subjects were coinfected with HIV representing 21.5%. Of all poly-resistant cases 2(1.5%) were seropositive to HIV as well as 17(12.6%) out of the 18 MDR-TB participants.

Table 1. Prevalence of HIV among DR-TB at NTBLTC Zaria

No. of Samples	**No. of DR-TB alone**	**Prevalence of coinfection (HIV +DR-TB)**
135	135(100%)	48(35.6)

Table 2. Distribution of HIV and DR-TB by Sex among Patients at NTBLTC, Zaria

Sex	**NO. Tested**	**DR-TB +/HIV+**	**DR-TB+/HIV**
Male	93	31	62
Female	42	17	25
Total	135	48	87

Table 3. Distribution of HIV+DR-TB among Patients by Age Demographics

AGE (Years)	**SEX Male No. (%)**	**Female No. (%)**	**Total**
01 – 09	0(00.0)	0(00.0)	0
10 – 19	0(00.0)	0(00.0)	0
20 – 29	12(25.0)	7(14.6)	19
30 – 39	9(18.8)	5(10.4)	14
40 – 49	4(8.3)	2(4.2)	6
50 – 59	6(12.5)	3(6.2)	9
60 – 69	0	0	0
Total	**31(64.6)**	**17(35.4)**	**48**

Table 4. Comparison of HIV Prevalence among Drug Resistant TB in Study Population

Resistant Type	**Frequency**	**HIV Positive (%)**	**HIV Negative (%)**
Mono Resistance (Rif)	115	29(25.2)	86(74.8)
Poly Resistance TB	2	2(100)	0(0.0)
MDR-TB	18	17(94.4)	1(5.6)
Pre-XDR-TB	0	0(0.0)	0(0.0)
XDR-TB	0	0(0.0)	0(0.0)

Discussion

Tuberculosis is a leading cause of death in people living with HIV [2]. Tuberculosis increases the progression of the disease in people living with HIV/AIDS and increases their susceptibility to active case of tuberculosis and drug resistant TB [12,26]

while HIV on the other hand is a major cause of failure of TB control efforts preventing TB control programs from reaching targets in high burden nations.[12]. HIV and TB coinfection heightens the risk of acquiring and harbouring MDR-TB strains.

In this study, the prevalence of HIV among drug-resistant TB subjects was determined to be 35.5%.

This finding is slightly higher than 26.7% and 14.29% reported in similar works on TB/HIV coinfection in Enugu and Kano [13,14] but compared sparingly with 29.27% and 32.8% reported in similar works at Olabisi Onabanjo University Teaching Hospital in Ogun state and a local community in Edo state [15,16].

One study report showed a lower overall prevalence of HIV/TB Coinfection of 7.6% [13] and another a 21.6% prevalence [17] which are all lower than the findings of this study.

Our findings are nonetheless consistent and comparable to 32.8% and 36.3% reported in some studies in Nigeria [18,19]. Other studies in Nigeria on TB/HIV coinfection have also reported high prevalence rates of between 28% and 43% [17,20].

A study in India reported a 4.42% HIV seropositivity among MDR-TB patients [21]. In Africa, countries such as Malawi and South Africa have a high prevalence of TB/HIV coinfection rates of between 56% - 62% [2,17]. The risk of developing TB in Sub-Saharan Africa is high [17] and up to 41% of TB cases in Africa were HIV coinfected [2].

According to USAID the prevalence of TB/HIV coinfection in Africa was 43% [22]. Possible reasons that may have accounted for the difference in the prevalence rates observed from other studies and ours may not be unconnected with the type of sample, study population and sample sizes used among other reasons. In our case, all study subjects were confirmed drug resistance TB patients out of which a spectrum were coinfected with HIV and not just mere TB/HIV coinfection alone.

We observed male dominance over females in terms of HIV seropositivity in the order of 23.0% and 12.6%. This finding is below the 2019 WHO report which states that 57% of all TB cases were seen in males [14,23,25,29]. The WHO report suggested that worldwide men were more at risk of being infected and suffering high mortality from TB than Women [13,25,29]. Some other studies reported higher TB/HIV coinfection rates among females than males [23,24].

The age group of 20-29 years had the highest rates of HIV seropositive cases determined to be 14.1% of the study population. This result compares with findings in Ethiopia and Northern India reported to have high male MDR-TB patients in the age group 24 representing 77.2% as against 56.9% and ages 21-45 years as against females in the same age group. [30]. This is followed by the age group 30-39 years which had 10.4%. The groups with the least cases were age range 50-59 and 40-49 found to be 6.7% and 4.4% respectively. No incidence of HIV seropositivity was however recorded in the Age ranges of 01-09 and 60-69. Our findings corroborate WHO's report which states that most TB cases occur among persons of age >15 [25]. We found the rate of coinfection with HIV based on the type of TB drug resistance to be 21.5% for monoresistance TB subjects while 1.5% and 12.6% were for poly-resistant and MDR-TB cases respectively.

Conclusion

The prevalence of HIV among drug-resistant TB subjects attending the National Tuberculosis and Leprosy Training Centre, Saye Zaria was found to be high. This finding has provided significant insights into the landscape of HIV+TB dynamics in the studied population. This should stimulate the urgency needed towards tailoring interventions and

enhanced diagnostic approaches to tackle the evolving dynamics of drug resistance.

Collaboration between healthcare professionals, policymakers, researchers, and the community at large is imperative to mitigate the burden of HIV/TB coinfection and to combat the emergence of drug-resistant strains effectively.

Conflict of Interest

I declare that there is no conflict of interest regarding the research presented in this paper. I affirm that I have not received any financial support and benefit or engaged in any commercial, legal, or professional relationship with other organizations, or with the people I am working with, that could influence this study.

Acknowledgements

The Authors Acknowledge the contributions of the management and the Health Research Ethics Committee of the NTBLTC as well as that of the staff members of the reference laboratory towards the success of this study.

References

[1] World Health Organization, 2015, (Guidelines on the management of latent tuberculosis infection), Date of access: 1 January 2015, Available from: https://www.who.int/publications/i/item/9789241548908.

[2] World Health Organization (Global Tuberculosis Report, 2014), Date of access: 23 October 2014, Available from: http://www.who.int/tb/publications/global_report/en/.

[3] DeCock, K.M., Soro, B., Coulibaly, I.M., and Lucas, S.B., 1992, Tuberculosis and HIV infection in sub-Saharan Africa. *JAMA*, 268:1581–1587. DOI:10.1001/jama.268.12.1581.

[4] Alikor, D. E. and Erhabor, N. O. 2006, "Trend of HIV- seropositivity among children in tertiary health institution in the Niger Delta Region of Nigeria*," Afr. J. Health Sci.* 13(1-2), 80-85. DOI: 10.4314/ajhs.v13i1.30820.

[5] Muhammad, K. M., Sana, R., Muhammad, A., Rizwan, I., Saqib, S., 2015, Comparison of Ziehl Neelsen Microscopy with GeneXpert for Detection of Mycobacterium Tuberculosis. *Journal of Dental and Medical Sciences*,14(11),56 - 60.https//www.iosrjournals.org.

[6] Theron, G., Peter, J., van Zyl-Smit, R., Mishra, H., Streicher, E., Murray, S., Dheda, K., 2011. Evaluation of the Xpert MTB/RIF assay for the diagnosis of pulmonary tuberculosis in a high HIV prevalence setting. *American journal of Respiratory and Critical Care medicine* 18(1).132-40. doi:10.1164/reem.201101-0056OC.

[7] Federal Ministry of Health, Federal Republic of Nigeria (Report: First National TB Prevalence Survey 2012, Nigeria), Date of access August; 2012. https://www.health.gov.ng/doc/First%20National%20TB%20Prevalence%20Survey%20Report.pdf

[8] World Health Organisation (Global Tuberculosis Report 2015), Date of access: 28 Oct 2015. www.who.Intltb/publications/global report.

[9] Boehme C.C., Nabeta P, Hillemann D., Nicol M.P., Shenai S., Krapp F., Allen J., Tahirli R., Blakemore R., Rustomjee R., Milovic A., Jones M., O'Brien S.M., Persing D.H., Ruesch-Gerdes S., Gotuzzo E., Rodrigues C., Alland D., Perkins MD., 2010, Rapid molecular detection of tuberculosis and rifampin resistance. *N Engl J Med.*,363(11):1005-15. doi: 10.1056/NEJMoa0907847.

[10] Hain Lifescience (GenoType MTBDRplus VER 2.0.) 2019, Identification of the M. tuberculosis complex and its resistance to Rifampicin and/or Isoniazid from pulmonary clinical specimens or cultivated samples.https://www.hain-lifescience.de/en/products/microbiology/mycobacteria/tuberculosis/genotype mtbdrplus.html.

[11] Federal Ministry of Health 2021, National AIDS and STDs Control Programme. National

Guidelines for HIV prevention treatment and care. https://nascp.gov.ng.

[12] Singh A., Prasad R., Balasubramanian V., Gupta N., 2020, Drug-Resistant Tuberculosis and HIV Infection: Current Perspectives. *HIV AIDS (Auckl)*,12:9-31. doi: 10.2147/HIV.S193059.

[13] Ugwu K.O., Agbo M. C., Ezeonu I. M., 2021, prevalence of tuberculosis, drug-resistant tuberculosis and hiv/tb co-infection in enugu, nigeria. *Afr J Infect Dis.* 15(2):24-30. doi: 10.21010/ajid.v15i2.5.

[14] Aminu A.I., Tukur A.D., 2016, Detection of multidrug resistant tuberculosis (MDR-TB) among rifampicin-resistant TB patients using line probe assay (LPA) in Kano, Nigeria, *Bayero J. Pure Appl. Sci.* 9 (2):1–8, https://doi.org/10.4314/bajopas.v9i2.1.

[15] Kolade O. R., Atilola O.G., Babalola T.V., Komolafe O.I., 2016, Prevalence of HIV infection among tuberculosis patients in a teaching hospital in South-West Nigeria: A four-year retrospective study, *science Direct HIV & AIDS Review*, 15,(4),136 - 140. https://doi.org/10.1016/j.hivar.2016.11.001.

[16] Oladeinde B.H., Olley M., Imade O.S., Onifade A.A., 2014. Prevalence of HIV infection among patients with pulmonary tuberculosis in a rural tertiary hospital in Nigeria. *Niger J Exp Clin Biosci*. 2:90-4. http://www.njecbonline.org.

[17] Adejumo O.A., Daniel O.J., Otesanya A.F., Adegbola A.A., Femi-Adebayo T., Bowale A., Adesola S., Kuku O.O., Otemuyiwa K.O., Oladega S.N., Johnson E.O., Falana A.A., Dawodu O., Owuna H., Osoba G., Dacosta A., 2017, Factors associated with tb/hiv co-infection among drug sensitive tuberculosis patients managed in a secondary health facility in lagos, nigeria. *Afr J Infect Dis.*11(2):75-82. doi: 10.21010/ajid.v11i2.10.

[18] Awoyemi O.B., Ige O.M., Onadeko B.O., 2002, Prevalence of active pulmonary tuberculosis in human immunodeficiency virus seropositive adult patients in University College Hospital, Ibadan, Nigeria. *Afr J Med Med Sci.* 31(4):329-32. https://pubmed.ncbi.nlm.nih.gov/15027773/.

[19] Egbe K., Ike A. C., Aleruchi C., 2016. Prevalence of Tuberculosis and Rifampicin Resistance Among Patients Seeking Medical Care in Nasarawa State, North Central Nigeria. *Science Journal of Public Health*, 4(3), 214-218. https://doi.org/10.11648/j.sjph.20160403.18

[20] Daniel O. J., Alausa O. K., 2006. Treatment outcome of TB/HIV positive and TB/HIV negative patients on directly observed treatment, short course (DOTS) in Sagamu, Nigeria. *Niger J Med.*,15(3): 222-6.doi: 10.4314/njm.v15i3.37217.

[21] Deivanayagam C.N., Rajasekaran S., Venkatesan R., Mahilmaran A., Ahmed P.R., Annadurai S., Kumar S., Chandrasekar C., Ravichandran N., Pencillaiah R., 2002, Prevalence of acquired MDR-TB and HIV co-infection. *Indian J Chest Dis Allied Sci.* 44(4):237-42. https://pubmed.ncbi.nlm.nih.gov/12437236/.

[22] United States Government agency for international development (The Twin epidemics: HIV and TB coinfection). https://2012-2017.usaid.gov/news-information/fact-sheets/twin-epidemics-hiv-and-tb-co-infection, Date accessed: June 2012 to September 2017.

[23] Gunda D.W., Maganga S.C., Nkandala I., Kilonzo S.B., Mpondo B.C., Shao E.R., Kalluvya S.E., 2018. Prevalence and Risk Factors of Active TB among Adult HIV Patients Receiving ART in Northwestern Tanzania: A Retrospective Cohort Study. *Can J Infect Dis Med Microbiol*. 4;2018:1346104. doi: 10.1155/2018/1346104.

[24] Kapata N., Chanda-Kapata P., Michelo C., 2013, The social determinants of tuberculosis and their association with TB/HIV co-infection in Lusaka, Zambia. *Medical Journal of Zambia*, 40 (2). https://www.ajol.info/index.php/mjz/article/view/110518.

[25] World Health Organization (Global Tuberculosis Report 2019), Date of access: 17 Oct. 2019. https://www.who.int/tb/publications/global_report/en/.

[26] Selwyn, P. A., Hartel, D., Lewis, V. A., Schoenbaum, E. E., Vermund, S. H., Klein, R. S., Walker, A. T., & Friedland, G. H., 1989. A

Prospective Study of the Risk of Tuberculosis among Intravenous Drug Users with Human Immunodeficiency Virus Infection. *New England Journal of Medicine*, 320(9), 545-550. https://doi.org/10.1056/NEJM198903023200901.

[27] Oshi, D.C., Oshi, S.N., Alobu, I., and Ukwaja, K.N., 2014, Profile, Outcomes, and Determinants of Unsuccessful Tuberculosis Treatment Outcomes among HIV-Infected Tuberculosis Patients in a Nigerian State. *Tuberc Res Treat*, http://dx.doi.org/10.1155/2014/202983.

[28] Njoku, A.K., 2005, Tuberculosis: Current Trends in Diagnosis and Treatment. *Nigerian Journal of Clinical Practice*, 8(2), 118-124.

[29] World Health Organization (who engages over 12,000 community informants fast-track efforts in finding 'missing TB cases), Date of access:23/03/2019.https://www.afro.who.int/news/who-engages-over-12000-community-informants-fast-track-efforts-finding-missing-tb-cases.

[30] Oladimeji, O., Atiba, B. P., Anyiam, F.E., Odugbemi, B. A., Afolaranmi, T., Zoakah, A. I., Horsburgh, C.R., 2023, Gender and Drug-Resistant Tuberculosis in Nigeria. *Trop. Med. Infect. Dis.*, 8, 104. https://doi.org/10.3390/tropicalmed8020104.